Mass Cytometry to Delineate the Human Muscle Stem Cell Hierarchy and Dysfunction in Aging

Grant Award Details

Mass Cytometry to Delineate the Human Muscle Stem Cell Hierarchy and Dysfunction in Aging

Grant Type: Basic Biology V

Grant Number: RB5-07469

Project Objective: To delineate the cellular hierarchy in human skeletal muscle and determine signaling networks that are disregulated in aged muscle stem cells (MuSC, defined as Lin- CD34+ CD20+ a7integrin+). In order to achieve this, the awardee will identify novel subsets of MuSC using multidimensional single-cell mass cytometry and then subsequently evaluate the specific cell populations' expression and properties at different periods of human aging.

Investigator:

Name:	Helen Blau
Institution:	Stanford University
Type:	PI

Human Stem Cell Use: Adult Stem Cell

Award Value: $1,175,357

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Mass Cytometry to Delineate the Human Muscle Stem Cell Hierarchy and Dysfunction in Aging

Public Abstract: Aging is characterized by a decline in skeletal muscle mass and strength (sarcopenia), coupled with an accumulation of fat tissue, impairing mobility and quality of life in 45% of individuals over 65 years of age. In aged mice, the regeneration defect arises in part from a diminished regenerative capacity of resident muscle stem cells (MuSCs). The goal of this proposal is to characterize muscle stem cell subsets residing in human skeletal muscle tissue and investigate the mechanisms responsible for their regenerative defects in aging. We will capitalize on two cutting edge technologies, single-cell bioengineered stem cell niches, which will allow tracking individual muscle cell fates, and multi-dimensional single-cell mass cytometry, which will allow resolution of the molecular characteristics of skeletal muscle cells from aged humans with detail previously unattainable. We expect that this combined approach will elucidate the functional defects observed in aged MuSC populations and therefore facilitate the development of a therapeutic agent to target muscle stem cells for the treatment muscle weakness in aged humans.

Statement of Benefit to California: The state of California is the front-runner in stem cell research, having gathered not only private investments, as demonstrated by the numerous biotechnology companies that are developing innovative tools, but also extensive public funds via Prop 71, that allows the state, through CIRM, to sponsor stem cell research in public and private institutions. In order to preserve its leadership position and encourage research on stem cells, the CIRM is calling for research proposals that could lead to significant breakthroughs or the development of technologies useful for studying stem cells in order to improve human health. Aging is characterized by a decline in tissue function and regenerative capacity that leads to degeneration and loss of muscle mass and strength (sarcopenia). Muscle stem cells (MuSCs), also known as satellite cells, are responsible for the maintenance and regeneration of skeletal muscle mass. Several studies have shown a decrease in MuSC function in aged mice. However, the mechanisms responsible for their reduced function are not yet defined. The work we propose here focuses on human muscle and discerning differences among subsets of muscle stem cells. The results will facilitate the development of targets to augment a muscle stem cell based therapy to treat muscle weakness in aged humans.